

JPRS: 3414

21 June 1960

MAIN FILE

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Price: \$0.50

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JPRS: 3414

CSO: 3785-D

HEMATOLOGY IN THE SOVIET UNION

[Following is a translation of an article by Ludvik Donner in Casopis Lekaru Ceskych, Vol XCIX, No 9, Prague, 26 February 1960, pages 44-47.]

II. Internal clinic of the faculty of general medicine of Charles University in Prague, Chairman Prof. Dr. FrHerles

On the basis of an invitation extended me by some Soviet hematologists I was sent in February 1959 by the Ministry of Education for a three-day study trip to the USSR. The purpose of the trip was to get acquainted with the work of Moscow and Leningrad hematologists. Work in hematology in the Soviet Union is primarily concentrated at the Institutes of Hematology and Blood Transfusion, which are situated in the majority of the main cities of the individual socialist republics. Hematological problems are also studied at some of the internal medicine clinics, however, on the whole less hematological work is done at the clinics than at the hematological institutes. All leading workers in the field of hematology have had two-year previous clinical experience in all of internal medicine, or perhaps are concurrently lecturing on internal medicine at the medical faculties. There is close cooperation with the field of blood transfusion, however both these fields are quite separate and problems relating to blood transfusion are not infrequently solved in much closer conjunction with the fields of surgery and internal medicine. There is no independent hematological society, however there are several special hematological sections within internal medicine societies. The journal common to all these groups is "Problemy gematologii i perelivaniya krovi" which comes out at the present time either in the Russian or English language twelve times a year.

The main centers of work in the field of Soviet hematology are: Central Institute of Hematology and Blood Transfusion in Moscow, and Institute of Hematology and Blood Transfusion, in Leningrad. The Moscow institute is composed of clinical parts, series of laboratories and division for blood donors. It employs about 700 people and the director of the institute is the academician prof. A.A. Bagdasarov, chief hematologists of the USSR, chairman of the internal medicine faculty of the pediatric branch. The clinical part has on the one hand a department for patients with various blood diseases (55 beds), on the other hand a

surgical division (95 beds). The patients with various blood diseases are admitted on the basis of recommendation of different clinics and hospitals in Moscow, however in greater number from other cities in the USSR; thus only about 25% of hospitalized patients comes from Moscow while the remainder is from the great variety of cities in the USSR. Admitting of the patients is governed by a special goal, since most of the admitted patients have the diseases that are currently being studied by the institute. To the clinical division is attached a large polyclinic with ambulatory investigations and therapy of patients with diseases of the blood. The surgical division works in close contact with the hematological clinic, and follows mainly the questions of blood transfer, blood replacement, significance of the spleen operations, conservation of bones, blood vessels and products of replacement of blood vessel walls.

The main theme of the hematological division of the institute, the bed division as well as the laboratory one is the problem of leukemia. Thus in the clinical division lie the most different kinds of acute and chronic leukemias and various phases of the disease, from various cities in the USSR. Leukemia is studied in the first place from the metabolic standpoint. By investigating a large number of indol substances in certain leukemias it was determined that indols are increased in this disease. With the aid of paper chromatography it was shown, that this increase is mainly conditioned by the increase in the level of oxy-5-indolacetic acid (Cassars and Mirzamamed). It is thought that the indol substances interfere with the production of tryptophane and in the plasma of leukemia patients tryptophane was increased while it was lowered in the leucocytes. Thus a hypothesis was advanced that (Dulcin and Sbecinska) in leukemia tryptophane is insufficiently utilized by the white blood cells. Apart from the metabolism of tryptophane there are other problems systematically studied in leukemias such as cytochemical questions, such as amount of fats, glycogen and nucleic acids in white blood cells (Terenteva). The interest in the question of leukemia stems also from the statistical analysis of 187 autopsied leukemia stems, where in the years 1945-1950 1.2% of autopsied material was leukemia, while in the years 1951-1958 it was 2.8%. (Bagdasarov, Nemenova and Malanina).

Apart from solving the pathogenesis of leukemia also better therapeutic methods are being sought. In a broad sense the chemotherapeutic effect is being studied. In acute leukemias when myeloblasts were present in peripheral blood the most effective agent proved to be 6-merkaptopurin of domestic manufacture, while the treatment with aminopterin was quite abandoned. In cases of chronic myelosis they administer mainly myleran of their own manufacture under the name of Mielosan. In isolated instances chronic myelosis is treated with Dopan, an alkylamine suitable for oral administration.

Apart from leukemia the clinic is interested in the pathogenesis of thrombocytemia either essential or secondary, observed at various time intervals following the removal of the spleen. They also follow

treatment of hemolytic anemias; there it was found that small to medium doses of prednisone were the most effective in hemolytic anemias together with repeated small doses of fresh plasma (Lorie and Paciora). In certain hypochromic hyposideric anemias with poor tolerance of iron medications they try blood transfer by using blood preserved with the aid of iron-changing substances (Dulcin and Feinstein). Certain problems of the clinic of the Moscow institute are concerned with aplasia and hypoplasia of bone marrow, of which in the course of several years 120 cases were observed at the Institute. Among them were described 5 patients with a special variant, where the normal number of thrombocytes was seen while at the same time the red and white cell count was low (Dulcin). The immunological interests of the clinic are concentrated on antibodies in acute aplastic anemias (Imnova, Lorie and Feinstein). Among other work of the clinical division it is also necessary to mention changes in the phagocytosis of leucocytes in experimental agranulocytosis (Feinstein) and follow-up of different types of macrocytic anemias (Cerncova).

The director of the clinical hematological division is prof. Dulcin who works with 11 other physicians: three senior scientific workers, seven younger scientific workers and one ordinary [intern]. The arrangement of the clinic does not differ from other hospital divisions, the wards have two beds up to eight beds, the majority of beds have arrangements for listening to the radio. Everywhere is absolute cleanliness and the patients can rest, read or play chess in special parts of the clinic, for the most part in wide corridors.

The individual research laboratories work in close cooperation with the clinical division. At the laboratories there are always chiefs, on the average 2 or 3 senior scientific workers, 4-5 younger scientific workers. Apart from cooperation with the clinic each laboratory independently works on solution of scientific problems. There are several laboratories and they form a kind of independent unit. There is a pathophysiological laboratory, biochemical laboratory, serological laboratory, bacteriological laboratory, cytological laboratory, laboratory of experimental leukosis, physical-colloidal laboratory, laboratory for clinical uses, for blood fractionation. An isotope laboratory is now being built. The cytological laboratory (Terenteva) is equipped with an electron microscope. There they study cells of leukemia in cultures of bone marrow, using mainly cultures in Carel's vessels or in a hanging drop. It also determines histochemical investigations, such as phosphatases, peroxidases, polysaccharides. It is particularly concerned with the changes in these substances in radiation diseases. The biochemical laboratory (Mesienev) studies the level of Vitamin B₁₂ in different blood diseases, is concerned with certain problems of coagulation and production of albumins following blood transfusions. In the laboratory of blood fractionation (mme) Rutberg studies the behavior of lipids of red blood cells when they are hemolyzed in vitro. She determined that phospholipids remain tied to the stroma of the red cells, while the cholesterol complexes are the most labile ones. This laboratory is also interested in certain questions pertaining to blood coagulation. They particularly studied effect of different concentrations

of calcium ion on the speed of coagulation of recalcified plasma. This laboratory also works on determination of properdin in different diseases and follows its levels particularly in radiation diseases. The director of the pathophysiological laboratory is Fedorov who is interested in the role of the stomach in creation of a blood-producing agent. He found that in dogs the main area when this agent is produced is the fundus and production depends on innervation of the stomach in the area where the stomach is irritated by food. In the laboratory of experimental leukemia Hausenbach studied the meaning of the nervous system in the transfer of leukemia, at the present time he is more interested in metabolic changes in experimental leukemias, which are of the type studied in the clinical department.

The central institute of hematology and blood transfusions is not the only place in Moscow which works in the field of hematology. In close cooperation with this institute are 2 internal medicine clinics of the pediatric branch which have been built in the rapidly expanding sector of south-western Moscow; these are the polyclinic of Prof. Bagdasarov and the clinic of Prof. Alperin. Both clinics are mainly concerned with the education of medical students, but some of the employees of the clinic are simultaneously employees of the institute, thus the cooperation is very close. In both clinics they study problems of reaction changes of white cell production in the source of several internal diseases, such as diseases of the liver, lungs and others. They are searching for the most suitable therapy of the thromboembolic states and are systematically trying out dicumarin, pelentan and phenylindandion which is produced locally. Also noteworthy are therapeutic successes of small doses of non-matching blood injected intravenously into patients with stomach ulcers.

In the suburb of Moscow in the Semasko hospital is employed one of the foremost Soviet hematologists J. A. Kassirskij. He is director of the clinic of the Institute for Completion of education of doctors where he is now working with prof. Aleksejev. Also in Kassirskij's department is Abramov, author of a monograph on cytology of different punctures. Kassirskij's school has been concentrating in recent years on the clinical picture of osteomyelosclerosis, for whose diagnosis they have commonly used both punctures and trepanations. In the last nine years they have observed 37 osteomyeloscleroses, where they noted at least 12 patients with bleeding. The chief task of the Kassirskij clinic is the completion of doctors' education in clinical matters. The study of hematology lasts 3 months, the doctor spends 2 hours daily independently in a morphological laboratory, spends 2 to 3 hours listening to lectures on hematology and spends the rest of his time at the bedside of the patient.

While Kassirskij rears hematologists primarily from the clinical standpoint, they obtain the laboratory view-point chiefly in the Botkino hospital, where the chairman of the internal department is the well-known hematologist prof. Kostova. The training takes place in the division

consisting of 25 laboratories, richly equipped with microscopes, automatic blood counting apparatus and other laboratory apparatus. Kostova has concerned herself for a number of years with pathogenesis of aplastic anemia, myelofibrosis, all of which she evoked in different experimental animals.

In Leningrad the hematology is primarily concentrated in the Institute of Hematology and Blood Transfusion, where the chairman is Doc. Beljakov, well known to us, who is concerned mainly with problems of blood preservation. The structure of the Institute is similar to the structure of the Central Institute of Hematology and Blood Transfusion in Moscow. The clinical part has a bed division for hematology and another one for surgery. The hematological part is directed by prof. Serman, and the surgical by prof. Filatov. The clinical hematological division is concerned just as the Moscow Institute primarily with the etiology and pathogenesis of leukemia. It follows the clinical and morphological picture of different leukemias, biochemical changes, chemotherapy, transfer of leukemia to experimental animals, relation of leukemia to the immune reaction, prepares experiments with transplants of bone marrow in leukemia. It works very closely with the childrens' clinic of prof. Tur, with the virus division of prof. Smorodina and with certain pharmacologists. The clinical division has 55 beds, the chief, 2 senior scientific workers, 4 junior scientific workers, 5 interns (?) and two undergraduates. The clinical work has confirmed the significance of the rtg therapy (roentgen ?) and chemotherapy (Serman, Kuzmin, Rozanova, Kyseleva). In the treatment of chronic leukemia the small effect of arzen was demonstrated, as well as toxicity of embichin and effectiveness of myleran and uretan in chronic myeloses. Great attention is paid to treatment of polycythemia with radioactive phosphorus (Rozanova). After almost 10 years of experience they recommend treatment per os in doses of 2 mc in repeated weekly rest-periods, total of three times. In patients with polycythemia they followed the favorable effect of repeated venepunctures on the activity of the cardio-vascular system, with the help of oscillography and sphygmography. In various blood diseases they investigated the amount of iron and catalase in blood plasma (Seitz). The lowest amounts of catalase were in patients with pernicious anemia, chronic lymphadenosis and acute leukemia. The increased amounts were in polycythemia.

Out of the work that was done mainly in the individual laboratories in close conjunction with the clinic, it is necessary to mention the observation that properdin apparently drops in the plasma of dogs following irradiation. The drop is in a direct ratio with the death of the animals. If zymozan is injected into the animal the level of properdin rises and a much smaller percentage of animals dies and also much slower than after a mere irradiation with rtg. At the present time they are studying the effect of zymozan on the bone-marrow. In rabbits following irradiation with rtg they evoked fatal leucopenia, which could be successfully averted by a preliminary transfusion of white cells (Teodorovic). Transfusions of white cells in the amount of 60-80 ml.,

repeated after several days, were successfully tried in cases of aleukemic leukemias, and lesser results were obtained in aplastic anemias and in agranulocytosis. By following the metabolism of glucose and lactate, tagged with radioactive carbon, they showed that acute leukemias, even if they have the same morphology, may have quite different glycolytic course in the white cells.

In the biochemical laboratory they follow the effect of anti-coagulating substances on individual agents of blood clotting (Kotovskikova). Besides pelentan and phenylindandion they also prepared 2-diphenylacetylindandion, as the so-called diphenacin, with an effect that lasts a long time and for several days. The laboratory of prof. Bogomolova is concerned with the original experiments, and also manufactures different therapeutic substances from blood. Thus there are different hemostatic sponges, biological antiseptic tampons, combined with anti-biotics, sterile serum for treatment of stomach ulcers, sterile serum from the blood of pregnant women for the treatment of arthritis. Besides this they prepare anti-anemic medicines, hemostimulin containing iron, copper and glucose, pherkoven- an intra-venous preparation, which contains iron, cobalt and glucose, they also test intramuscular preparation of iron, copper and manganophermin. The laboratory also prepares thrombin, fibrinogen, antihemophilic globulin, blood substitutes, dextran, hydrolysates of albumins and dried plasma.

In Leningrad at the clinic of Prof. Tusinsky (internal medicine) it is prof. Jarasevskij who works on the hemetological problems. We know him from his publications on the meaning of the central nervous system in the composition of the total white blood cell picture.

At the present time he is trying to prove the significance of the nervous system particularly the spleen, on the action of erythropoietin. At the clinic of internal diseases of the Kirov military academy, where Botkin used to work, the substitute for Arinkin is his student prof. Beier. He has been following with the aid of radio-active iodine the activity of the thyroid gland in different types of leukemia and lymphogranuloma. He found that in acute leukemia and chronic myelosis there is increased activity of the thyroid gland, while in lymphogranulomas it is lowered. Besides this his clinic is studying the relation of embryonic blood formation in the liver and in the spleen, to the pathogenesis of the leukemic rampant growth in adult life. The above mentioned centers of work do not begin to exhaust all the hematological centers in Moscow and Leningrad. I only mention the ones that were visited. I have spoken to the majority of the mentioned workers, I have heard their hypotheses and have suggested to them my own work problems. In Moscow at the Institute of Hematology and Blood Transfusion I lectured in Russian before 250 listeners concerning the investigation of blood clotting with the help of thromboelastography. I was also the chairman at the meeting of the Moscow hematological division and took part in the debate.

Previously I had taken charge of combined symposia of the hematologists of the socialist countries.

The comparison of Moscow and Leningrad hematology is favorable to Leningrad, where the work is directed toward a clearer goal. Hematology here is not as suppressed by concern for blood transfusion, foreign work is here better known and here they use modern methods, which are just beginning to be introduced in Moscow.

Soviet workers in the field of hematology are critically aware of some these minor handicaps and have great respect for the work of Czechoslovak hematologists, whose publications they mostly know quite well. When we compare our hematology to the level of Soviet hematology we see that Soviet physicians concentrate more only on some of the most important problems of hematology, while the Czechoslovak hematologists are trying to work on a whole series of hematological problems both simultaneously and with equal emphasis. Our work approach lacks the intensity of work and leads to greater dispersal of work, however it enables us to maintain the level of Czechoslovak hematology as a unit on a level with all other subdivisions. If we compare the study of hematology in Czechoslovakia and USSR, we will note the insufficiency of our teaching methods. Descriptive tables with charts, drawings, microphotographs, whole series of microscopes, spacious laboratories all point to the fact that in this direction our teaching of hematology whether of medical students or of average public health personnel is very inadequate.

The work opportunities of Soviet hematologists are remarkable from several standpoints. They are so well financed that pay from just one work center is quite sufficient therefore they have no interest in additional earnings. Their work is highly valued socially, therefore they enjoy respect that is almost inconceivable under our conditions. They are afforded complete peace and concentration on work, which in spite of the fact that it is regularly checked, does not get distracted by a series of other duties, which are performed instead by less qualified scientific or public health forces. Good laboratory equipment a six-hour work day, and finally protection of scientific workers from all disturbing influences, visits and telephone calls, permits a degree of concentration essential for productive work, whose amazingly positive results are more and more evident in the specialized scientific literature.

Submitted: 30/9/1959

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